REMARKS

Reconsideration is respectfully requested in view of Applicants' amendments and remarks herein.

First of all, correction of clerical error has been made in amended claim 1.

The claims under consideration are claims 1-3 and 6-8.

Applicants appreciate the withdrawal of the previous rejections as set forth throughout the Office Action. Two rejections remain. It is believed that in view of the comments set forth below and enclosures submitted herewith, that the remaining rejections are overcome and all claims are in condition for allowance.

At the bottom of page 2 of the Office Action, claims 1-3 and 6-8 are rejected under the first paragraph of 35 U.S.C. § 112 as based on a non-enabling specification.

Although Applicants disagree with the approach of the Examiner, in that, they again submit that any demonstrated utility or any utility accepted by the skilled artisan from understanding the disclosure is sufficient to fulfill the enablement requirement, the present specification when taken in conjunction with the knowledge of one of ordinary skill in the art, does enable the claimed transgenic mammals for use in xenotransplantation. Thus, even considering the more strict position of the Examiner, the claims are still enabled.

The Examiner maintains that the art of xenotransplantation is unpredictable with respect to suppression of hyperacute rejection in organ transplant recipients. The Examiner questions whether it is predictable if hDAF/CD55 will be expressed at a level and specificity to allow xenotransplantation of transgenic organs by preventing hyperacute rejection.

Applicants submit herewith WO 97/12035 published April 3, 1997 which date is prior to Applicants' Japanese priority application filing date. WO '035 is directed to transplanting organs, etc. with suppression of complement activation and reduction in severe immune reaction following transplantation of the donor organ.

Although the "invention" of WO '035 is directed to the co-use of an enzyme which may reduce the level of antigenic Galα (1,3) Gal or gal epitope and a complement inhibitor such as CD59, this reference includes sections directed to the production of transgenic non-human mammals only expressing the human CD59 protein and testing of the transplanted heart from transgenic pigs. The transplantation was made into the baboon. Regarding the preparation of the transgenic mammal expressing only the complement inhibitor, see section D beginning at page 54 of WO '035 where first the transgenic pig containing only the complement inhibitor is prepared. Next, note page 69 thereof, full paragraph on discussing the transplantation of the pig heart into the baboon and the results obtained. This xenotransplantation data states that the grafted hearts continue beating 2.25 and 3 hours, respectively, which was "slightly" longer for non-transgenic pig hearts (0.5 to 1.5 hours). (quotation marks not in original) However, at page 69 beginning at line 20, the disclosure thereon goes on to state that the transgenic xenografts exhibit evidence of resistance to complement-mediated injury and appear relatively normal 2 hours post graft reperfusion. Endothelial cells were stated to be appearing undamaged, with little evidence of myocyte injury and with only few platelet thrombi.

From consideration of WO '035, the skilled artisan certainly understands that transgenic mammals expressing a complement inhibitor such as DAF are useful in xenotransplantation.

Please note that although the above specific exemplification of the reference is with respect to complement inhibitor CD59, WO '035 also discusses DAF as well as MCP.

In further support of their position, Applicants also encloses herewith WO 91/05855. As explained at the top of page 10 of the '855, methods are provided for transplanting animal tissue into a recipient with a donor species being discordant with respect to the recipient, while providing in association with the grafted tissue one or more homologous complement restrictive factors active in the recipient species to prevent the complete activation of complement. The purpose of course is to prevent a hyperacute rejection. The homologous complement restriction factors (HCRFs) useful in WO '855 are inclusive of those considered in WO '035, that is CD59, DAF and MCP. For example, see pages 13 and 17 of WO '855.

Without question, the skilled artisan would accept that as of Applicants' priority application date., the art of xenotransplantation was at least predictable enough so that the skilled artisan would accept suppression of hyperacute rejection in organ transplant recipients utilizing an organ from the transgenic non-human mammal as claimed herein. Demonstrated practical utility for "permanent" use in a human recipient is not necessary to meet the utility and enablement requirements of the first paragraph of 35 U.S.C. § 112. Acceptance of utility in the baboon experiment is sufficient. Accordingly, it is requested that the 35 U.S.C. § 112 first paragraph rejection be reconsidered and withdrawn.

At the top of page 6 of the Office Action, claims 1-3 and 6-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rosengard et al. taken with Toyomura '474.

With respect to this rejection, Applicants enclose herewith a Certified English Translation of their Japanese priority application 9/205235 filed July 14, 1997, thereby antedating the 102(e) date of November 17, 1998 of Toyomura '474. Applicants also note that the filing date of their Japanese application is prior to the PCT publication date of Toyomura (November 27, 1997).

Applicants respectfully submit that their Certified English Translation of priority application supports their claims under the first paragraph of 35 U.S.C. § 112. In this regard, a mammal, mouse, is utilized in the examples thereof carrying a promoter PMCP up stream of DAF/CD55. See claim 3 at page 3 and at page 7. An active promoter region of PMCP is inherent in PMCP itself. See last paragraph on page 11 of the Certified English Translation regarding expression in organs and tissue. This includes the endothelial cells of claims 2 and 3. From the Background portion of the Certified English Translation, especially section [0003] at pages 4-5, it is clear that the purpose of the Japanese priority application is to carry out the experimentation in the described transgenic mice, for translation into pigs. This supports present claims 4 and claim 5. Claim 8 is supported by the Sequence Listing of the Certified English Translation.

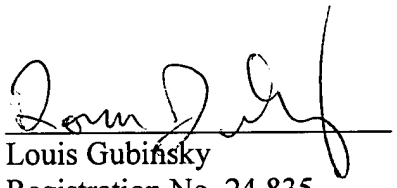
From the above, Applicants respectfully request withdrawal of the 35 U.S.C. § 103(a) rejection.

Applicants enclose herewith an alternate 1449 listing the two PCT publications discussed herein.

It is believed this application is now in condition for allowance. If any minor points remain prior to Notice of Allowance, the Examiner is respectfully requested to contact the undersigned at the below listed phone number

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims are amended as follows:

1. (Twice Amended) A transgenic non-human mammal comprising a gene of a human complement inhibitor (DAF/CD55) and a promoter, of the porcine complement inhibitor (PMCP), defined by Sequence ID No. 1 or a part thereof, at an upstream locus, said promoter or part thereof promoting expression of the human complement inhibitor (DAF/CD55), and said mammal expressing the human complement inhibitor in an organ or tissue.